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Supreme Court, U. S.
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IN THE

SUPREME COURT OF THE UNITED STATES

OCTOBER TERM, 1973

NO. 73-1563

RANDALL RAY GRANT,

Petitioner.

V.

THE STATE OF TEXAS

PETITION FOR A WRIT OF CERTIORARI TO THE COURT OF CRIMINAL APPEALS OF THE STATE OF TEXAS

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April 15, 1974

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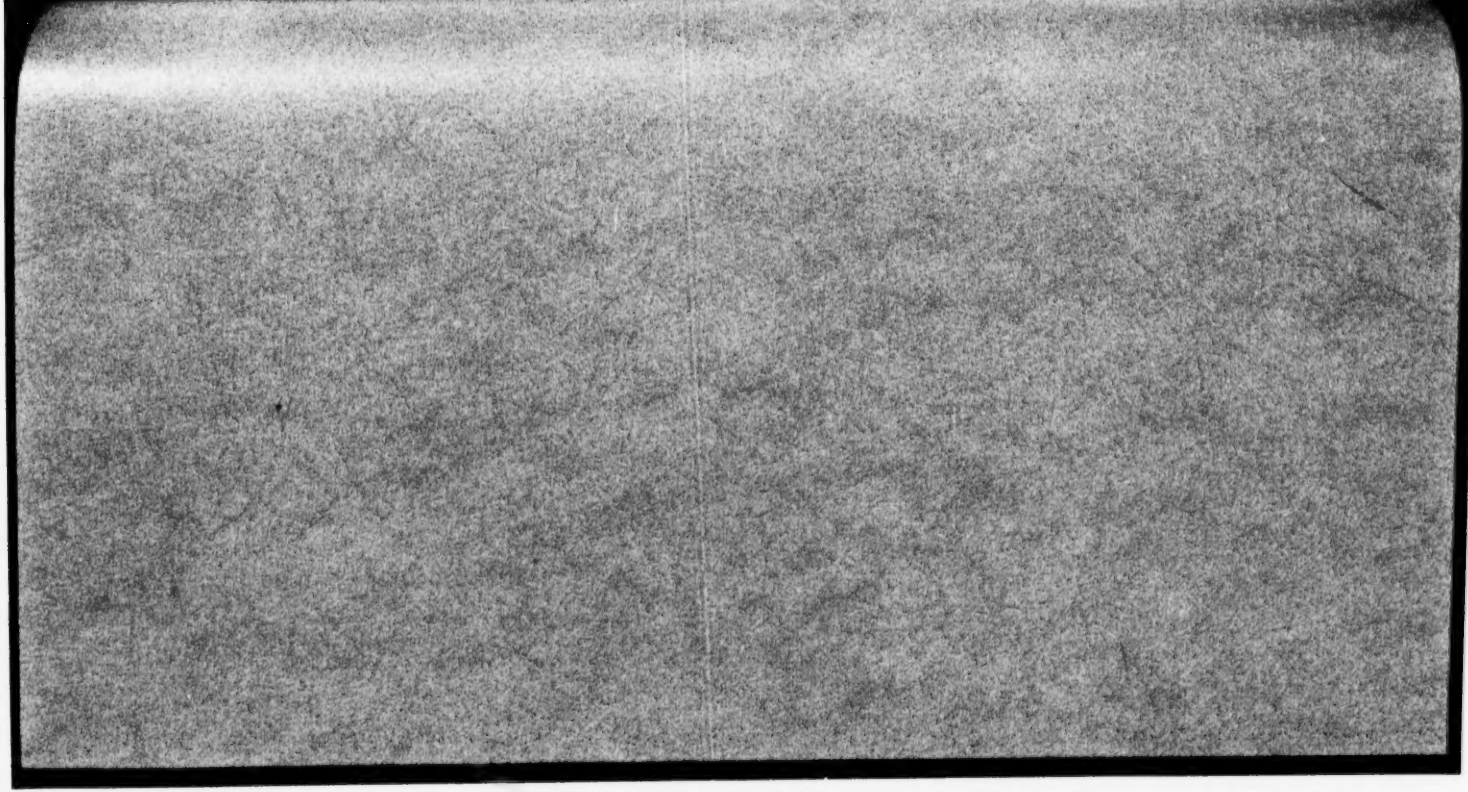

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THE STATE OF TEXAS

PETITION FOR A WRIT OF CERTIORARI

TO THE COURT OF CRIMINAL APPEALS
OF THE STATE OF TEXAS

The petitioner, RANDALL RAY GRANT, prays that a writ of certiorari issue to review the opinion and judgment of the Court of Criminal Appeals rendered in these proceedings on February 27, 1974.

OPINIONS BELOW

The opinion of the Court of Criminal Appeals of Texas appears in 505 SW2d 279, and is Appendix I hereto. Trial Courts do not render written opinions in Texas.

JURISDICTION

The court of Criminal Appeals of Texas delivered its opinion herein on February 6, 1974. That Court then denied leave to file Appellant's Motion for Rehearing on February 27, 1974 and issued its mandate on March 1, 1974. (Appendix II)

The jurisdiction of this Court is invoked under 28 USC, § 1257 (3).

QUESTION PRESENTED

Texas has different criminal penalties for motor vehicle operators who do so while under the influence of debilitating substances. For alcohol influenced operators (DWI), first offense is a misdemeanor and jail sentence is mandatory; felony penalties are mandatory on subsequent convictions. For "drug" influenced operators (DUID) all penalties are only misdemeanor; jail sentence is permissible and felony penalties are never imposable. (Appendix III)

Alcohol is itself a drug, even a narcotic drug.[1] (Appendix IV)

1. May Texas, by statutory scheme, classify and impose different penalties on motor vehicle operators who do so while under the influence of a debilitating substance, i.e., alcohol or some "other drug," without showing an appropriate governmental interest suitably furthered by such differential treatment?

CONSTITUTIONAL PROVISION INVOLVED

Constitution of the United States, Amendment XIV, § 1

". . . [N]or shall any state . . . deny to any person within its jurisdiction the equal protection of the laws."

---

[1] Whether alcohol is a drug or some other debilitating substance, the question is the same.

STATEMENT OF FACTS

Petitioner was arrested and charged with misdemeanor driving under the influence of alcohol.

At the trial of his case, (DWI) petitioner filed pleadings showing the repugnancy between the two schemes the State of Texas has for punishing motor vehicle operators who operate motor vehicles while under the influence of debilitating substances. The evidence showed that alcohol is itself a narcotic drug, but that Texas law ignores such fact and ascribes a greater penalty for alcohol influenced motor vehicle operators than it does for "drug" influenced motor vehicle operators.

The State offered nothing to show any appropriate governmental interest suitably furthered by such differential treatment. Neither did the State attempt to show that drivers under the influence of alcohol are any more dangerous to the traveling public than are drivers under the influence of any other drug. No appropriate governmental interest in the differential treatment can be imagined.

HOW FEDERAL QUESTION WAS RAISED AND PASSED ON

Petitioner, in Trial Court, raised the question of unequal protection of the laws by the State's imposing different penalties for what is actually the same behavior. (S of F, p. 26, paragraphs 7, 8, 9, 10, 13, 14, and 15) By his Motion for New Trial, filed in Trial Court after conviction, he laid the basis for appeal. (Tr. pp. 13 and 14, paragraphs 11 and 12)

The Texas Court of Criminal Appeals found that petitioner's contention of denial to him of equal protection of the laws, while "ingenious [was] specious" and was without merit. This opinion was handed down the 6th day of February, 1974 and the Court of Criminal Appeals denied Petitioner's Motion for Leave to File Motion for Rehearing on February 27, 1974.

REASONS FOR GRANTING THE WRIT

The Court below has decided a federal question of substance in an way probably not in accord with applicable decisions of this Court.

The Texas Scheme

The Texas scheme of penalizing motor vehicle operators who do so while under debilitating substances is as follows:

ALCOHOL (DWI)	*DRUG* (DUID)
Art. 802 P.C.	Art. 6701d, Sec. 50 (a) and (b) V.A.T.S.
FIRST Offense (MISDEMEANOR)	*FIRST Offense* (MISDEMEANOR)
3 days in jail (mandatory) - 2 years in jail and $50.00 - $500.00 fine[1]	10 days in jail (discretionary) - 2 years in jail or $50.00 - $500.00 fine or Both jail and fine
Art. 802b P.C.	
SECOND Offense (FELONY)	*SECOND Offense*
10 days in jail - 2 years in jail or $100.00 - $5,000.00 fine or Up to 5 years in penitentiary	Same as first offense (Never a FELONY)

[1] Potential felony conviction is also a part of the penalty received in all misdemeanor DWI cases.

It is readily apparent that Texas does not penalize all debilitated motor vehicle operators the same. Even in the misdemeanor DWI cases, three days of jail time is mandatory, whereas in the DUID cases jail time is only permissive. Further, there is no felony DUID penalty.

Petitioner concedes that equal protection of the laws does not mean all persons must be dealt with identically. *Marshall* v. *United States*, —— U. S. ——, 94 S.Ct. 700, 38 L.Ed. 2d 618 (1974) and cases therein cited. But if a State distinguishes between members of a class, such distinction must have a rational relation to a legitimate state purpose. *Weber* v. *Aetna Casualty Company*, 406 U.S. 164, 92 S.Ct. 1400, 31 L.Ed. 2d 768 (1972)

The crucial question in dealing differently with members of a class is whether there is an appropriate governmental interest suitable furthered by such differential treatment. *Police Department of City of Chicago* v. *Mosley*, 408 U.S. 92, 92 S.Ct. 2286, 33 L.Ed. 2d 212 (1972). The question, therefore, becomes what is the "appropriate governmental interest" that Texas has in either of the statutes?

The declared purpose of Texas' DWI law is to prevent men, women and children from being wounded and maimed by persons driving automobiles while intoxicated. *Johnson* v. *State*, 147 SW2d 811. Texas' purpose in the DUID law, as set out in the statute itself, is "safety". Article 6701d, Sec. 50(a), V.A.T.S. Therefore, the purpose of each statute is the same, i.e., safety on the highways.

The question then becomes whether or not an alcohol intoxicated motor vehicle operator is more dangerous on the highway than a "drug" intoxicated motor vehicle operator?

The very asking of the question illustrates the fallacy of the Texas scheme. Are the Courts to presume that an alcohol influenced motor vehicle operator is more dangerous on the highways than is an opium influenced operator? Is one drug influenced driver more dangerous than another? The invidiousness of the discrimination is attenuated when one reflects that alcohol is itself nothing more or less than a narcotic drug. (Appendix IV and see S of F, p. 92, *et. seq.*)

The State of Texas has failed to show it has an appropriate governmental interest in setting different punishments for what is actually the same offense. Not all persons in the same class, under the Texas scheme, are subjected to the same potential punishment. Texas is denying alcohol (a narcotic drug) influenced motor vehicle operators equal rights to those accorded to "other drug" influenced motor vehicle operators. For example, jail sentence is mandatory for alcohol influenced operators but only discretionary for "drug" influenced operators. Thus, Texas, by its scheme, violates the equal protection clause of the 14th Amendment of the United States Constitution. *Mosley, supra; Weber, supra.*

Prosecutor Discrimination

As the statutes in question are worded, a prosecution for alcohol influenced drivers may be begun under either statute. This is so because alcohol itself is a narcotic drug. Thus, a prosecutor, because of whim, political favor, or in an effort to prevent a potential felony conviction[1], may, at his peculiar choice, elect to prosecute the traditional DWI case as a DUID case. No one could complain.

Under such circumstances, even if the law were non-discriminatory on its face, it is grossly discriminatory in its operation. *Williams* v. *Illinois*, 399 U.S. 235, 90 S.Ct. 2018, 26 L.Ed. 2d 586. And if it may be applied in such a way as to violate the equal protection clause, it does so violate it. *Yick Wo* v. *Hopkins*, 118 U.S. 356, 6 S.Ct. 1064, 30 L.Ed. 220.

Thus, these discretionary statutes are unconstitutional in their operation. They are pregnant with discrimination and discrimination is an ingredient not compatible with the idea of equal protection of the law. *Furman* v. *Georgia*, 408 U.S. 238, 92 S.Ct. 2726, 33 L.Ed. 2d 346 (1972) Douglas, concurring.

---

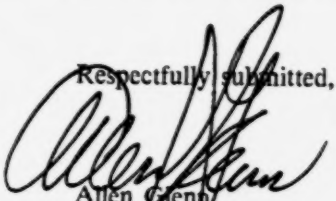
[1] Felony conviction has far ranging consequences to persons who engage in licensed professions.

The Texas scheme of penalizing one type of drug influenced driver different from another driver under another type of drug has no justification legally or factually. It has shown no appropriate governmental interest in making such discrimination, nor can it do so. The statutes are grossly discriminatory in operation.

CONCLUSION

For these reasons, a writ of certiorari should be issued to review the judgment and opinion of The Court of Criminal Appeals of Texas.

Respectfully submitted,

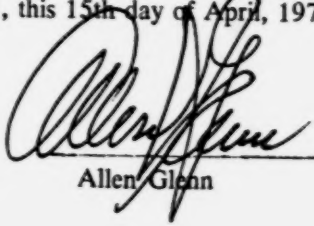


Allen Glenn
P. O. Box 1316
Abilene, Texas 79604

April 15, 1974

CERTIFICATE OF SERVICE

This is to certify that I have mailed true and correct copies to the State's attorneys, Bob Lindsey, Assistant District Attorney of Taylor County, at the Taylor County Courthouse, Abilene, Texas 79602 and Jim Vollers, State's Attorney, P. O. Box 12405, Austin, Texas 78711, this 15th day of April, 1974.



Allen Glenn

APPENDIX I

RANDALL RAY GRANT, Appellant
NO. 47,643 APPEAL FROM TAYLOR COUNTY
THE STATE OF TEXAS, Appellee

OPINION

The offense is driving while intoxicated; the punishment, a fine of $150 and ten days in jail with the jail sentence probated for a period of six months.

Appellant was arrested by Department of Public Safety Officers Morgan and Pueschel after a high-speed chase of several miles. He was arrested and taken to the departmental headquarters in Abilene where a breathalyzer test was conducted. Both officers testified that appellant was intoxicated and Officer Morgan testified that this fact was confirmed by the results of the breathalyzer test. Appellant was then taken to the county jail and placed in the custody of the sheriff. The arrest took place on December 23, 1972, at a time when the courthouse was closed for the Christmas holidays. On December 27, Officer Morgan filed the complaint forming the basis of the information upon which appellant was convicted in this case.

On December 28, Officer Morgan filed a complaint in the Justice of the Peace Court of Precinct 3 of Taylor County wherein appellant was charged with the offense of driving and operating a motor vehicle on a public street or highway, on December 23, 1972, "at the unreasonable, imprudent and unlawful speed of 100 + miles per hour" in a 65 miles per hour speed zone. Officer Morgan testified that both offenses occurred at the same time; i.e., appellant was intoxicated while driving in excess of 100 miles per hour in a 65 miles per hour zone.

In March, 1973, after some prodding from Officer Morgan, appellant appeared before the Justice of the Peace, entered a plea of guilty to the speeding complaint, was found guilty, assessed a fine of $50 and court costs, and actually paid such fine. The DWI charge came on for hearing thereafter and appellant filed a lengthy plea of double jeopardy setting out such facts. The plea was supported by his affidavit and had attached thereto certified

copies of the proceedings in the Justice of the Peace Court. The trial court overruled the plea and it now forms the basis of ground one.

Appellant relies upon the double jeopardy provision of the federal constitution, the fifth amendment made applicable to the states under the fourteenth amendment, Benton v. Maryland, 395 U.S. 784, 23 L.Ed. 2d 707, 89 S.Ct. 2056 (1969). He also cites Waller v. Florida, 397 U.S. 387, 25 L.Ed. 2d 435, 90 S.Ct 1184 (1970), as well as Benard v. State, 481 S.W. 2d 427 (Tex. Crim. App. 1972). Accepting the teachings of all of these authorities, we disagree with the contention advanced. Nor are the cases cited on the doctrine of carving in point under the fact structure of the case at bar.

Instead, we find that the well-written opinion of McMillan v. State, 468 S.W. 2d 444, 445 (Tex. Crim. App. 1971), to be dispositive of the contention of appellant. In *McMillan*, the defendant was seen driving on the wrong side of the street; and, when he was stopped, was found to be intoxicated. He was charged in the municipal court with driving on the wrong side of the street, pleaded guilty and paid his fine. Later, he was convicted of DWI—almost our precise fact situation.

Art. 802, V.A.P.C., dealing with the offense of driving while under the influence of intoxicating liquor, does not provide for a lesser included offense of driving at an unreasonable and excessive rate of speed. McMillan, supra, and authorities therein cited. Accord: Evans v. State, 479 S.W. 2d 282 (Tex. Crim. App. 1972); Sutton v. State, 495 S.W. 2d 912, 915 (Tex. Crim. App. 1972), Crabb v. State, —— S.W. 2d —— (No. 47,233, 1/9/74). Ground one is overruled.

Next, by grounds two and three, appellant advances an ingenious but specious, contention that Art. 802, P.C., is inoperative because it is in conflict with Art. 6701d, § 50 (a), V.A.C.S., the statute prohibiting the operation of a motor vehicle over the public streets and highways while under the influence of drugs. He offers as a factual basis for his argument long excerpts from a book on pharmacology which he introduced while examining a pharmacist tendered as a witness. He refers us to statements from this book supporting his thesis that "alcohol is a narcotic drug in

that it acts on the central nervous system as a depressant." We reject the contention so advanced.

> The pertinent part of § 50 (a) reads:
> "It is unlawful for any person who is under the influence of any narcotic drug or who is under the influence of any other drug to a degree which renders him incapable of safely driving a vehicle to drive a vehicle within this state."

Art. 802, P.C., makes it a misdemeanor for a person to operate a motor vehicle upon the public streets or highways of the state "while such person is intoxicated or under the influence of intoxicating liquor."

We do not find the two statutes to be in conflict nor do we agree with appellant that Art. 802 was repealed by implication since § 50 (a) was enacted at a later date.

The two statutes are not repugnant. Art. 802 applies only to the driving of a motor vehicle on the public streets, alleys, or highways while intoxicated or under the influence of intoxicating liquor. § 50 (a) prohibits the driving of a motor vehicle within the state when (1) the operator is under the influence of any narcotic drug; or (2) the operator is under the influence of any other drug to a degree which renders him incapable of safely driving a vehicle. Each is a separate and distinct offense governed by a separate statute, and proof that an accused has violated one would be insufficient to support a conviction under the other. See Frazier v. State, 480 S.W. 2d 375, 380 (Tex. Crim. App. 1972), wherein the Court said: "[T]he possession of a dangerous drug is not the same criminal act as the possession of a narcotic drug."

This Court, over an extended period of time, has held that the words "intoxicated" and "while under the influence of intoxicating liquor", as used in Art. 802, are of common understanding and do not need to be defined. 1 Branch's Ann. P. C. (2d ed) § 15, p. 10 (1956). A study of the cases cited, as well as those subsequently decided, shows clearly that the common understanding refers to the drinking of intoxicating liquor, not the ingestion of drugs as ordinarily spoken of in the everyday affairs of the people. Cf. *Davis v. State*, 142 Tex. Crim. 602, 155 S.W. 2d 801, 803 (1941).

Repeals by implication are not favored. Ex parte Spann, 122 Tex. Crim. 314, 54 S.W. 2d 510, 512 (1932). As was said in Berry v. State, 69 Tex. Crim. 602, 156 S.W. 626, 635-636 (1913):

> "A statute is repealed by implication whenever it becomes apparent from subsequent legislation that the Legislature does not intend the earlier act to remain in force, and the converse of this proposition is that no statute will operate as an implied repeal of an earlier statute, if it appears that the Legislature did not intend it so to operate."

Finding no inconsistency between the two statutes, grounds two and three are overruled.

Finally, appellant contends that the prosecution under Art. 802 denies to him rights equal to those who may be prosecuted under § 50 (a) because there is no felony offense of driving while under the influence of drugs, while a second offender under Art. 802 may be so prosecuted. Preliminarily, we do not find that appellant has standing to urge the invalidity of the classification since he has been convicted only of the misdemeanor offense. Facing the issue head on, we find no merit in the ground and it is overruled.

The fixing of penalties and punishment for offenses under the penal laws of this state is within the exclusive domain of the legislature and not of the courts. Sasser v. State, 131 Tex. Crim. 347, 98 S.W. 2d 211 (1936); David v. State, 543 S.W. 2d 172, 179 (Tex. Crim. App. 1970).

The judgment of the trial court is affirmed.

QUENTIN KEITH, Commissioner

(Delivered February 6, 1974)

Opinion approved by the Court

APPENDIX II

CLERK'S OFFICE, COURT OF CRIMINAL APPEALS
OF TEXAS
AUSTIN, TEXAS

I, TOMMY LOWE, Chief Deputy Clerk of the Court of Criminal Appeals of Texas, do hereby certify that in Cause No. 47,643, styled:

RANDALL RAY GRANT,

Appellant

VS.

STATE OF TEXAS,

Appellee

the judgment of the Court at Law of Taylor County, Texas, was affirmed on February 6, 1974, leave to file appellant's motion for rehearing was denied on February 27, 1974 and on March 1, 1974 the mandate issued.

THEREFORE, with the denying of the leave to file appellant's motion for rehearing, this cause was disposed of by this Court on February 27, 1974, and the appellant having exhausted all remedies in this, the Court of Criminal Appeals of Texas, said judgment has now become final on the docket of this Court.

WITNESS my hand and seal of said Court, at office, in Austin, Texas, this 5th. day of April, A. D. 1974.

(SEAL)

(Signed)

TOMMY LOWE, Chief Deputy Clerk
Court of Criminal Appeals of Texas

APPENDIX III

Art. 802. Driver intoxicated or under influence of intoxicating liquor

Any person who drives or operates an automobile or any other motor vehicle upon any public road or highway in this State, or upon any street or alley within the limits of an incorporated city, town or village, while such person is intoxicated or under the influence of intoxicating liquor, shall be guilty of a misdemeanor and upon conviction shall be punished by confinement in the county jail for not less than three (3) days nor more than two (2) years, and by a fine of not less than Fifty ($50.00) Dollars nor more than Five Hundred ($500.00) Dollars. Provided, however, that the presiding judge in such cases at his discretion may commute said jail sentence to a probation period of not less than six (6) months. Acts 1923, 2nd C.S., p. 56; Acts 1935, 44th Leg., 1st C.S., p. 1654, ch. 424, § 1; Acts 1937, 45th Leg., p. 108, ch. 60, § 1; Acts 1941, 47th Leg., p. 819, ch. 507, § 1; Acts 1953, 53rd Leg., p. 480, ch. 167, § 1.

Art. 802b. Subsequent offense of driving while intoxicated; felony

Any person who has been convicted of the misdemeanor offense of driving or operating an automobile or other motor vehicle upon any public road or highway in this state, or upon any street or alley within an incorporated city, town or village, while intoxicated or under the influence of intoxicating liquor, and who shall thereafter drive or operate an automobile or other motor vehicle upon any public road or highway in this state, or upon any street or alley within the limits of an incorporated city, town or village, while such person is intoxicated or under the influence of intoxicating liquor, shall for each and every subsequent such

violation be guilty of a felony; and upon conviction shall be punished by a fine or not less than One Hundred ($100.00) Dollars nor more than Five Thousand ($5,000.00) Dollars or confinement in the county jail not less than ten (10) days nor more than two (2) years, or by both such fine and imprisonment, or by confinement in the state penitentiary not to exceed five (5) years. Added Acts 1941, 47th Leg., p. 819, ch. 507, § 2, as amended Acts 1951, 52nd Leg., p. 813, ch. 457, § 1.

Art. 6701d

ARTICLE V—DRIVING WHILE UNDER THE INFLUENCE OF DRUGS AND RECKLESS DRIVING

Persons under the influence of drugs

Sec. 50. (a) It is unlawful for any person who is under the influence of any narcotic drug or who is under the influence of any other drug to a degree which renders him incapable of safely driving a vehicle to drive a vehicle within this state. The fact that any person charged with a violation of this Section is or has been entitled to use such drug under the laws of this state shall not constitute a defense against any charge of violating this Section.

(b) Every person who is convicted of a violation of this Section shall be guilty of a misdemeanor and shall be punished by confinement in the county jail for not less than ten (10) days nor more than two (2) years, or by fine of not less than Fifty ($50.00) Dollars nor more than Five Hundred ($500.00) Dollars or by both such fine and imprisonment.

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APPENDIX IV

Pharmacology and Therapeutics
By Arthur Grollman and Evelyn Grollman

3. The Aliphatic Alcohols

ETHYL ALCOHOL

When sugar-containing juices undergo fermentation, ethyl alcohol is formed according to the following reaction:

$$C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2$$

Glucose Alcohol

The intoxicating effect of spontaneously fermenting fruit juices was discovered by primitive man and such beverages have been used from the earliest times. Although of minor importance as a drug, ethyl alcohol is of considerable pharmacologic interest because of its widespread use.

Alcoholic liquors are generally prepared by the fermentation of sugars, which either exist preformed in the fruits or are derived from starch by a preliminary ferment action. Wines and beers generally contain only a low percentage of alcohol (2 to 20 per cent). The stronger preparations (*spirits*) are prepared by distillation, which raises the percentage to 30 to 60 per cent and at the same time removes the non-volatile constituents. Spirits and liquors are not, however, simple mixtures of alcohol and water but contain many other volatile substances. During the process of fermentation, a mixture of higher alcohols (n-propyl, isopropyl, n-butyl, isobutyl, n-amyl, isoamyl, etc.) are also formed which constitute the *fusel oil* ("bad liquor") of naturally fermented liquors. These are converted to their esters during the process of aging and impart to the final product much of its distinctive flavor and bouquet.

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Alcoholic Intoxication

In small quantities, as a rule, alcohol produces a feeling of well-being and good fellowship, along with increased confidence in the powers, mental and physical, of the subject of the experiment, as so-well expressed by the poet Horace when he wrote:

"What wonders does not wine! It discloses secrets; ratifies and confirms our hopes; thrusts the coward forth to battle; ceases the anxious mind of its burden; instructs in the arts. Whom has not a cheerful glass made eloquent! Whom not quite free and easy from pinching poverty!"

Larger quantities are followed by a certain amount of excitement, marked by laughter, loquacity, and gesticulation. The face becomes flushed and hot, the eyes brighter and livelier; the pulse is accelerated. Even at this stage, self-control is partially lost and the willpower is weakened. The speech may be brilliant, but it often betrays the speaker; the movements are more lively, but they are often undignified. The loss of self-control is often indicated further by furious outbursts of anger and unreasonableness or by the indulgence in maudlin sentimentality and sensual fancies. The sense of responsibility and the power of discrimination between the trivial and the important are lost, and the individual has no regard for the feelings of others or the ordinary conventions of life. If the bout be further continued, the movements become uncertain, the speech becomes difficult and stammering, the walk becomes a stagger, and a torpid slumber follows. Often nausea and vomiting set in, although these are entirely absent in some cases. On awakening from slumber, there is great depression with nausea, vomiting and anorexia, which may last for several days, associated with the symptoms of acute gastrointestinal irritation.

Very large quantities of alcohol lead to a deep, torpid sleep which eventually passes into total unconsciousness, resembling the condition in anesthesia; the respiration becomes stertorous and slow, and the face, which has hitherto been flushed, becomes pale or cyanotic. This condition may last for several hours and end in death from failure of the respiration, but in other cases the anesthesia becomes less deep and after a very prolonged sleep the pa-

tient recovers. When the stage of anesthesia is reached, it lasts much longer than that produced by chloroform or ether. If unconsciousness lasts longer than ten to twelve hours, recovery is unlikely.

The effects of alcohol differ a good deal in individuals as well as in the same individual at different times. One person is rendered sentimental, another bellicose, while in a third there may be no appearance of excitement, the first distinct symptoms being profound slumber. When drinking is indulged in in company, the excitement stage is a very common phenomenon, but if alcohol is taken without the exhilarating accompaniments of bright lights and exciting companionship, it is much less frequently seen.

The confidence in their own powers exhibited by intoxicated persons and their apparent fluency of speech are not evidence of a stimulant action on the brain but result from a loss of habitual shyness and nervousness. Experienced speakers, who are not averse to alcohol, indulge only sparingly, if at all, when they have to make a speech in which they require their full faculties. Alcohol in moderate doses always has a depressant effect on the motor and mental faculties. Thus the speed and strength of the knee-jerk and of reflex closure of the eyelids are lessened by 30 ml. of alcohol in man indicating that the reflex arc responsible for these movements is depressed. The amount of work and endurance of soldiers on the march and of mountain climbers is also reduced by the administration of small amounts of alcohol. Work requiring skill (*e.g.*, marksmanship, piano playing, typesetting, etc.) is also done with more error and with lesser endurance following the administration of alcohol. The special senses (sight, hearing, touch) and neuromuscular coordination generally are much less keen following the ingestion of even small quantities of alcohol than normally. Psychologic experiments have also failed to demonstrate any stage of accelerated nervous activity or of an initial stimulant action on the brain and have shown only a depression following the ingestion of alcohol. It is only where alcohol removes nervousness, selfconsciousness and anxiety by depression of the higher inhibitory centers that it may contribute to better performance.

In the lower parts of the central nervous system, the primary depression induced by alcohol leads to interference with the coordination of the finer movements even with doses of alcohol which do not perceptibly affect the speech and walking. Skilled work is performed more slowly and far more errors occur than in normal conditions, and lead to serious accidents.

Because of its exciting and stimulating effects, it was formerly believed that alcohol first stimulates and then depresses the nerve cells. However, the error of this view is now generally recognized, for alcohol, like the anesthetics described in the preceding chapter, depresses the central nervous system from the beginning. The stimulation observed following the ingestion of alcohol is comparable to the excitement produced by the general anesthetics and is a result of the removal of the inhibitory effects of the cortex and the weakening of the highest functions of the brain—the will and self-restraint. *Even the smallest quantities of alcohol tend to lessen the activity of the brain, the drug appearing to act most strongly, and therefore in the smallest quantities, on the most recently acquired faculties to annihilate those qualities that have been built up through education and experience, the power of self-control and the sense of responsibility. Alcohol must be considered pharmacologically as a narcotic which depresses first the highest cerebral centers, and then the lower ones including the cerebellum and spinal cord.*

The question of the action of small amounts of alcohol upon the central nervous system has assumed great importance because of its role in the causation of automobile accidents. Obvious drunkenness as manifested by staggering gait and impaired speech is easily recognizable but even small amounts of alcohol which produce no signs of gross intoxication are sufficient to render a driver highly dangerous upon the public highway. Chemical tests for alcohol in the blood or urine may be employed for such purposes since in general one can, as shown in Table 3-1, correlate behavior reactions with the alcoholic content of the body fluids. An arbitrary amount of 0.02 per cent of alcohol in the blood has been frequently quoted as being capable of interfering with the proper handling of an automobile while 0.2 per cent (1 mg. per liter in the expired air) indicates definite intoxication. Many in-

dividuals exhibit clinical evidence of intoxication at blood levels of 0.1 per cent and decreased competence at 0.015 per cent. The blood level of alcohol attained is about 0.001 per cent for each milliliter consumed, so that the ingestion of as little as one ounce of whiskey or one-half pint of beer will result in a blood level of 0.01 per cent, which suffices to exert a definite intoxicant effect.

Concentration of alcohol in blood (per cent)	*Behavior reactions*	*Concentration of alcohol in urine (per cent)*
<0.1	Apparently normal but slight changes detectable by special tests	<0.1
0.1 to 0.2	Emotional instability; slight motor incoordination	0.1 to 0.25
0.2 to 0.35	Confusion; staggering gait; slurred speech	0.25 to 0.45
0.3 to 0.4	Stupor	0.35 to 0.55
0.35 to 0.55	Coma	0.5 to 0.7
>0.55	Death	>0.5

A level of 0.15 per cent of alcohol in the blood has been considered as evidence of being "under the influence" of alcohol but specialists agree that no one is fit to drive a motor vehicle when the blood alcohol level is 0.1 per cent, a level now adopted by several of the states as evidence of intoxication. In Norway, a blood level of 0.05 per cent is considered as presumptive evidence of intoxication, a level which impairs the driving ability of many individuals. To attain this level, the average adult must consume at least two 12-ounce bottles of beer or 2 ounces of 100-proof whiskey.

In general, the concentration of alcohol in the blood is 1.2 times as high as in the brain; 0.8 as high as in the urine and 2000 times as high as in the expired air. It reaches its maximum blood level within an hour after ingestion.

Absorption and Excretion

Alcohol diffuses readily through the gastrointestinal tract and is rapidly equilibrated in the tissues. About 20 per cent of that ingested is absorbed through the stomach, the remaining 80 per cent from the small intestine, principally, the duodenum. Alcohol is absorbed at a rate proportional to its concentration in the gastrointestinal tract. Dilution, therefore, results in a slower rate of absorption as does also the ingestion of alcohol with food which delays the emptying time of the stomach. This is particularly true if the food is high in fat content. Alcohol is also readily absorbed from the peritoneum and through the lungs but not through the skin.

After absorption, alcohol disappears from the blood at a rate of 15 mg. per 100 ml. per hour. For a 150-pound individual, this means the metabolism of approximately 7 grams or the amount present in two-thirds of an ounce of whiskey, hourly. The rate at which alcohol disappears from the body is sufficiently constant to permit a calculation of how long after a given dose the body will be alcohol-free and to estimate with reasonable accuracy what the blood concentration was a few hours before a blood analysis was made. This rate of disappearance of alcohol cannot be accelerated by exercise, by increasing the metabolic rate, or by the administration of vitamins or drugs acting on the kidney, circulation, or central nervous system. In mice, however, heavy muscular exercise increases the rate of metabolism of alcohol up to 8 per cent and in man the ingestion of fructose also accelerates its rate of utilization.

More than 90 per cent of the alcohol ingested is metabolized, the remainder being excreted unchanged by the kidneys and lungs. The amount excreted by the kidneys is proportional to the volume of the urinary secretion, alcohol passing through the kidney by simple diffusion. The amount excreted through the lungs can be increased slightly by hyperventilation. Traces of alcohol appear in the sweat and milk.

Pharmacologic Action

The pharmacologic effects of alcohol are dependent primarily upon (1) its irritant action locally; (2) its action on the central

nervous system; (3) its metabolic and caloric functions; and (4) its action on various parenchymatous organs.

Local Action. The local irritant action of ethyl alcohol is due to the partial precipitation of the proteins of the cells and to its dehydrating property. This is shown by the results of its application to the skin, to wounds, and to mucous membranes. Applied to the skin in sufficient concentration (*e.g.*, 60 to 90 per cent), it produces redness, itching, and a feeling of heat like other volatile and irritant substances such as the volatile oils. Alcohol is, however, much less irritant and at the same time more volatile than these so that when placed on the intact skin it evaporates rapidly and produces a sensation of cold and little or no irritant action. This is especially true when dilute alcohol is used since no very distinct appearances of irritation of the skin are produced by solutions under 40 to 50 per cent. On ulcers and other unprotected surfaces, the irritant action is much greater, and its application is attended by pain and smarting. The precipitation of the proteins lends alcohol an astringent action but if it penetrates deeper, it may destroy the cells, and it then becomes a corrosive until it is diluted by the tissue fluids.

Its effects on mucous membranes are similar to those on wounds. In the mouth, strong alcohol produces a burning, unpleasant sensation which passes to the throat and stomach when it is swallowed, and if the concentrated vapor be inhaled, it causes irritation and reflex closure of the glottis.

Nervous System. Depression of the nervous system, as already indicated, is the principal pharmacologic action of alcohol and the basis for its use. It also causes a prolonged secretion of cerebrospinal fluid and raises the pressure in the subarachnoid space, which account in part for its after-effects attributed to gastric disturbance and the cerebral edema or "wet brain" observed at autopsy in subjects dying of acute alcoholism. Alcoholic "staggers" are a consequence of disturbances in both cerebellar and vestibular function. The latter causes a positional and gaze nystagmus which is useful in gauging the intensity of intoxication and may be prolonged for 24 to 48 hours after an alcoholic debauch.

Alcohol first depresses the ascending reticular-activating system, the more primitive part of the brain, thereby releasing the cortex from its integrating control and leading to loss of the finer grades of discrimination, memory, concentration, and insight. The spinal reflexes are first enhanced being freed from cerebral inhibition, followed by generalized impairment of nervous function and ultimately by general anesthesia. The electroencephalogram reveals slowing of the brain wave rhythm.

The cutaneous vasodilitation and flush which accompany the ingestion of alcohol in man is a result of central vasomotor depression. The respiratory and circulatory centers of the medulla preserve their functions after complete unconsciousness and disappearance of the reflexes have occurred. The effects of alcohol on the respiration are small and inconstant.

Circulation. Alcohol accelerates the heart rate but this is secondary to the excitement which it induces and not to any direct action on the heart. Even small amounts of alcohol (15 ml.) may, in those unaccustomed to taking alcoholic liquors, cause a transient acceleration of the pulse and cardiac output and a slight rise in arterial pressure. This is a reflex effect from the mouth and throat. When moderate amounts (30 ml.) of alcohol in a diluted form are given occasional drinkers, there is a slight rise in pulse rate coming on in from 15 to 30 minutes and not dependent upon psychic factors which might produce such changes in non-drinkers immediately after alcohol has been taken. In moderate drinkers, slightly larger amounts (35 ml. or more) cause appreciable increases in both blood pressure and in cardiac output (Fig. 3-1). Alcohol is believed by some to augment the strength of the heart, but the change is small in extent and inconstant in its appearance. Larger quantities affect the heart in the same way as ether and chloroform, weakening the auricular and later the ventricular systole and inducing dilatation and slowing of both chambers. The action of alcohol on the heart is much less, however, than that of chloroform and ether, much more being required to arrest the frog's heart, and the mammalian heart continues to beat when perfused with 2 per cent alcohol.

Peripheral dilatation in the skin is one of the prominent effects of moderate doses of alcohol and is responsible for the sensa-

tion of warmth induced by taking alcoholic beverages. A similar action on cerebral vessels has been observed but the intravenous administration of ethyl alcohol in sufficient amounts to raise the blood alcohol level as high as 0.2 per cent is without significant effect on the blood flow, metabolic rate, and vascular resistance of the brain. Severe alcoholic intoxication, delirium tremens and chronic alcoholism are associated with the marked reduction in the cerebral circulation and metabolism characteristic of all types of coma.

In dogs, the intravenous administration of alcohol causes a marked increase in the work load of the heart which is proportional to the amount administered. The coronary blood flow is decreased with an increase in resistance of the coronary arteries. It is apparent, therefore, that the action of alcohol on the circulation is such that it is impossible to regard it as a basis on which serious therapeutics can be founded. The ingestion of large

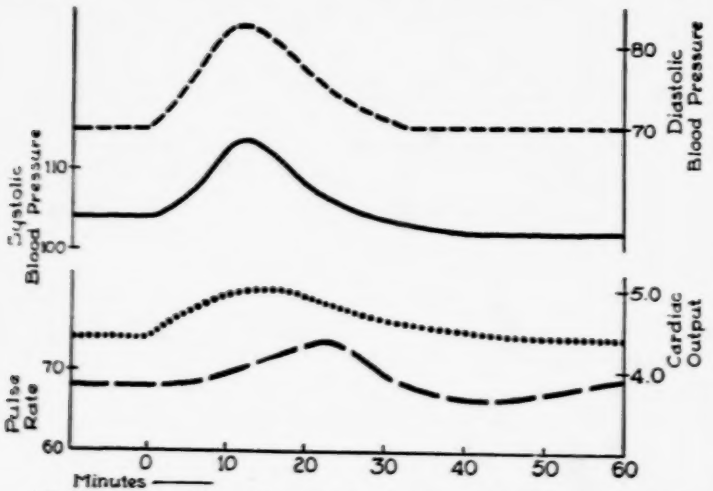


Fig 3-1. The effect of ethyl alcohol on the circulation. At the time indicated as O, an amount of whiskey equivalent to 35 ml. of alcohol was administered. Changes in cardiac output, pulse rate and systolic and diastolic blood pressure are indicated as ordinates (Grollman).

amounts or its chronic use may lead, as indicated later, to serious cardiomyopathy.

Liver. Alcohol exerts a direct effect on the liver inducing hyperlipemia (with an increase in serum triglycerides and free fatty acids) and ultimately in a fatty liver. This effect is believed to be a consequence of the increased concentration of DPNH induced by alcohol which decreases the rate of utilization of triglycerides. Alcohol may also interfere with the synthesis of lipoprotein, accelerate the mobilization of fatty acids from adipose tissue, increase the synthesis of fatty acid, and inhibit the release of triglycerides from the liver. The relative role of each of these factors is uncertain. In rats the hepatic concentration of long chain acetyl-CoA derivatives and of α-glycerol phosphate are increased. The acute fatty liver induced by ethanol in this species may be inhibited significantly by the prior administration of an antioxidant (α-tocopherol).

Digestive Tract. The effect of alcohol on digestion has been the subject of many investigations, both from the clinical and the experimental point of view. There exists a widespread belief in both lay and medical circles that small quantities of alcohol taken before a meal increase the appetite while after food they accelerate the digestion. It is obvious that alcohol may affect digestion either by altering the activity of the ferments in the digestive canal or by altering the secretion, movement, or absorption of the stomach and intestine. The digestive power of the gastrointestinal ferments is not altered *in vitro* when pure alcohol is present in small quantity. However, when amounts in excess of 20 per cent are added, the peptic activity of gastric juice is reduced and secretion is retarded. The ingestion of wines and beer in small amounts may increase the psychic secretion of the gastric juice. Liquors having a high concentration of alcohol (20 to 50 per cent) exert a carminative effect. Excessive amounts of alcohol decrease the secretion of intestinal and pancreatic juices and cause hyperemia and the secretion of a thick mucus.

The presence of alcohol in the mouth causes a very appreciable increase in the secretion of the saliva, presumably by reflex action. A similar increase in gastric secretion has been attributed to the liberation of histamine and of gastrin from the antrum

of the stomach, which acts in addition to the local reflex and psychic effects. Ethyl alcohol in concentrations below 10 per cent exerts little effect on the motility of the stomach and intestines; in concentrations above 15 per cent the motility and secretions are reduced. The ingestion of large quantities (50 ml.) in high concentrations induces irritation of the gastrointestinal tract with a profuse secretion of mucus. This is responsible for the nausea, vomiting and other symptoms of gastritis which follow the ingestion of alcohol.

Kidney. Alcohol alters renal function in several ways. It induces a diuresis in part as a result of the ingested fluid as well as by depressing the secretion of the antidiuretic hormone. The diuresis induced by alcohol is not accompanied by a concomitant excretion of salt and hence the body fluids become hypertonic. Alcohol also increass the urinary excretion of magnesium several fold, with a lesser increase in the excretion of calcium, but decreases the excretion of potassium. The mechanism of this action is unknown but it may be responsible for the hypomagnesemia observed in alcoholics. Alcohol withdrawal results in a "rebound" increase in the secretion of antidiuretic hormone.

Other Effects. Alcohol induces many metabolic changes in the organism which are believed to be a result of the deranged DPN:DPNH(NAD:$NADH_2$) ratio induced by the drug. There is an increased production of lactic acid which, in turn, reduces the urinary excretion of uric acids. The latter effect accounts for the precipitation of an attack of gout after indulgence in alcohol.

Alcohol also alters the metabolism of serotonin and the catecholamines. The metabolism of norepinephrine is altered from its usual oxidative to a reductive pathway. There is a significant increase in urinary norepinephrine, dopamine and metanephrine.

Large doses of ethanol also increase the splanchnic blood flow, the rate of oxidation of galactose, and the plasma glucocorticoid levels. In rats, a single dose of ethanol given intraperitoneally increases the activity of δ-aminolevulinate synthetase in the liver which may be responsible for the increased excretion of coproporphyrin induced by alcohol in man. In addition to these immediate metabolic disturbances, secondary to $NADH_2$-NAD

shifts, delayed changes in intermediary metabolism may also occur.

The effect of alcohol in intermediary metabolism accounts probably for the deaths which occasionally follow the ingestion of barbiturates after the ingestion of alcohol.

The ingestion of alcohol is occasionally followed by an allergic reaction. It is not established whether alcohol itself acts as an allergen in these cases, whether the reaction is due to some ingredient of the alcoholic beverage, or whether the alcohol enhances an already existing allergic disposition.

Metabolism

The liver is the principal organ concerned in the metabolism of ethanol. Kidney, lung, diaphragm and brain slices have a limited capacity to oxidize ethanol *in vivo* but contribute only slightly to its total metabolism in the intact animal. The major pathway for the metabolism of ethanol is by oxidation to acetaldehyde and acetate as depicted in Figure 3-2, but other pathways such as oxidation by catalase, the formation of ester sulfates, the formation of 5-hydroxy-4-ketohexanoic acid, and other reactions may play a minor role. It has been shown, for example, that β-D-glucosiduronic acid is a metabolite of ethanol in rat and man.

The initial step in the metabolism of ethanol, as shown in Figure 3-2, is its hydrogenation to acetaldehyde, a reaction catalyzed by a zinc-containing enzyme, alcohol dehydrogenase, using diphosphopyridine nucleotide (variously designated as DPN or NAD) as the hydrogen acceptor. This initial oxidative step is the rate-limiting reaction in the metabolism of ethanol. Since the supply of DPN is limited, the rate of utilization of ethanol is influenced by the concentration of ethanol only at levels below 0.01 per cent. At this blood level, the concentration of alcohol decreases exponentially with time; at higher levels, it decreases linearly. DPN (or NAD) is reduced to DPNH (or $NADH_2$) in the process of oxidation of alcohol and must be constantly reoxidized which explains why the administration of such substances as pyruvate, fructose or aminoacids may increase the rate of oxidation of ethanol.

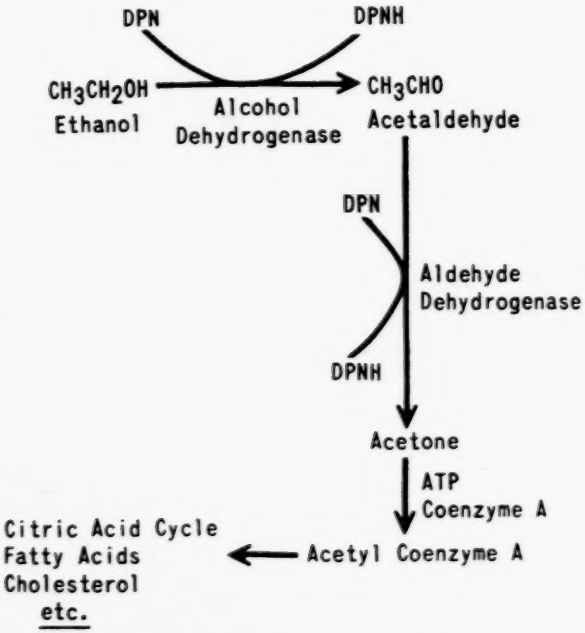


Fig. 3-2. Major pathway for the metabolism of ethanol.

There is good evidence to indicate that factors other than the activity of hepatic alcohol dehydrogenase and the availability of DPN are concerned in the metabolism of ethanol. Nor is it entirely certain whether all the acetaldehyde is oxidized to acetate as shown in Figure 3-2 or whether it forms acetyl coenzyme A directly. In any case, the acetyl coenzyme A formed may be oxidized to CO_2 and H_2O, the ultimate catabolites of ethanol, or may be added to the metabolic pool and be utilized in various anabolic reactions involved in the synthesis of cholesterol, fatty acids or other tissue constituents.

Hypoglycemia. Hypoglycemia after alcohol ingestion, although uncommon, is an important complication, appearing usually after a period of fasting. Vulnerability to the hypoglycemic effect of alcohol is observed in subjects with deficient activation of gluconeogenesis in starvation or accelerated diversion from the postprandial metabolism of carbohydrate and protein to the starvation metabolism of fat. In such subjects hypoglycemic reactions to alcohol can be demonstrated after an overnight fast.

Is Alcohol a Food? In man only 5 per cent or less of the ingested alcohol is excreted while the rest undergoes combustion in the tissues. In this process, alcohol furnishes energy to the body and, therefore, is technically a food, but this does not imply that it is a desirable one. Alcohol, therefore, acts as a substitute for carbohydrate and fat in the food and is utilized like them for the production of heat and work, each gram of alcohol ingested supplying 7.1 calories. The ingestion of 60 ml. (2 ounces) of 90 proof whiskey supplies 190 calories while a liter of beer containing 4 per cent alcohol, would supply about 230 calories.

Like fat and carbohydrates, alcohol exerts a sparing action on endogenous protein utilization as may be demonstrated by determining the nitrogen balance on diets in which part of the calories are furnished by alcohol. When alcohol is given in addition to a diet adequate in caloric value, nitrogen excretion is reduced, indicating a sparing action on proteins (*see* Fig. 3-3). Alcohol accordingly can take the place of some of the fat and carbohydrate in the food, and leads to the same economy of protein as do other constituents of the diet. It is this capacity of alcohol to serve as a food that leads to obesity in those who imbibe considerable amounts of alcoholic beverages in addition to an adequate diet.

When sufficiently large quantities of alcohol are taken, the resulting depression and sleep are accompanied by a decrease in general metabolic exchange due to decreased muscular movement. The opposite effect is seen during the excitement stage. The slight fall in body temperature (rarely more than 0.2 to 1° C.) observed after the administration of alcohol is a result of the greater output of heat from the dilated blood vessels of the skin.

There is a greater fall in the temperature after alcohol than in normal conditions following exposure to cold. This may be in part a result of the dilatation of the skin vessels but probably is due chiefly to the temperature-regulating mechanism being rendered less sensitive by alcohol.

The fall in temperature produced by alcohol is generally accompanied by a feeling of heat, and a thermometer applied to the skin may actually show a rise of several degrees because more blood flows through the dilated vessels. If much excitement and movement follow the ingestion of alcohol, no fall in the temperature may result, the increased heat formed during the movement compensating for the increased output, and in some cases, a rise of temperature occurs from the same cause. Very large quantities of alcohol may lead to a fall in temperature of 3 to 5°

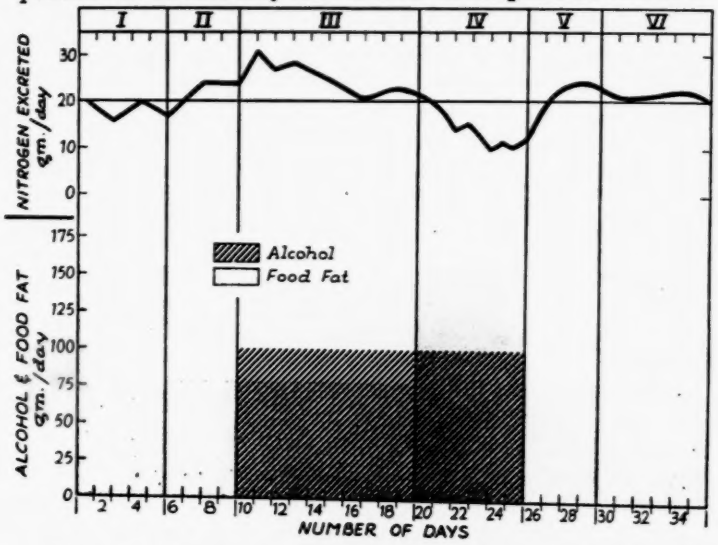


Fig. 3-3. The effect of alcohol on nitrogen elimination. The wave-line represents the nitrogen excreted. It rises rapidly in the second period when the fat of the food was reduced to one-half, but soon falls in the third period when alcohol was substituted. 100 grams of alcohol is chemically equivalent to 78 grams of fat. (After Neumann.)

C., owing in part to the lessened movements during unconsciousness.

Other Effects. Although much has been written on the effects of the chronic use of alcohol on growth and progeny, there is no good evidence to indicate that alcohol causes an heritable deterioration of the offspring. However, one might anticipate that the underlying instability and constitutionally psychopathic inferiority responsible for alcoholism in the parent might be transmitted to the progeny.

There is no good evidence to indicate that alcohol directly decreases the resistance of an individual to infection. However, the chronic alcoholic will usually suffer from dietary deficiencies which will secondarily lead to lowered resistance, and to degenerative changes in the gonads and other parenchymatous organs.

Repeated doses of alcohol produce tolerance so that larger doses are required to induce the same pharmacological effect. However, this tolerance is lost after abstinence for several months. Habituation to alcohol does not modify its rate of absorption or metabolism nor is there any correlation between the degree of tolerance and the condition of the liver. Tolerance to alcohol reflects an adaptation of the central nervous system to the state of intoxication rather than an alteration in the rate at which the alcohol is metabolized.

Patients suffering from *Hodgkin's disease* are reported to note pain at the site of their lesions following the ingestion of alcohol. The mechanism of this reaction is unknown.

Alcohol is generally credited with aphrodisiac powers, that is, with increasing sexual desire, but as Shakespeare (Macbeth, act 2, scene 3) correctly noted: "Lechery, sir, it provokes, and unprovokes; it provokes the desire, but it takes away the performance." The tendency toward sexual excess observed in intoxication is due not to any effects on the generative organs but to the loss of self-control from the action of the poison on the brain.

Chronic Alcoholism

Alcoholism has become an important social and economic problem which it is estimated affects five million people in the United States. The term is now used to include all who are ad-

dicted to the use of alcohol to such a degree that it interferes with their health, personal relations, social adjustment, and economic efficiency. Alcoholism thus constitutes one of the major diseases of modern life. The habitual indulgence in alcohol to excess is a consequence of its action on the brain in numbing the consciousness of unhappiness. This weakening of the higher sensibilities by drink is generally the object sought by the drunkard. He finds that under the influence of alcohol his habitual depression disappears, he loses the sense of degradation and remorse which possesses him when sober, he attains a spurious courage and he is inspired with a sense of adequacy which he normally lacks. As so aptly expressed by Samuel Johnson: "In the bottle discontent seeks for comfort, cowardice for courage and shyness for confidence." The depression and sense of frustration and inadequacy return in exaggerated form after the effects of the drug have passed off, but it can be removed again by the same means, and in this way the habit is formed, each successive dose being rendered necessary by the depression produced by its predecessor. This descent into chronic drunkenness is facilitated by the lessening of the self-control, owing to the action of alcohol on the brain. The victim may form the best of resolutions, but his impaired will-power and self-control are unable to carry them out. The depression in mood of the chronic alcoholic has been attributed also to depletion of serotonin and norepinephrine from the brain stem. The concentration of these neurohormones, to be described later, are reduced following the chronic ingestion of alcohol.

The first symptoms of chronic alcoholism are usually referred to the gastrointestinal tract, throat, and larynx and consist of chronic inflammation, accompanied often by such affections of the skin as dilatation of the cutaneous vessels (especially of the face), acne, and pustular eruptions. With continued abuse of alcohol and particularly when accompanied by nutritional deficiency, many serious complications appear involving the nervous system, liver, heart, muscles and other organs.

Nervous System. Alterations of the central nervous system lead to impairment of memory, self-control, and other higher mental processes. Tremor, convulsive attacks, hallucinations, and

mania not uncommonly follow, once the disease is well established. A form of amblyopia commencing with atrophy of the retinal ganglion cells and later extending to the fibers of the optic nerve may occur; it is much more readily elicited by methyl than by ethyl alcohol. The neuritic symptoms occurring in chronic alcoholism resemble those seen in beriberi and are due to thiamine deficiency. Such patients may rapidly improve when this deficiency is remedied even though their alcohol intake may still be continued.

Chronic alcoholism results also in functional and organic changes in the brain. The latter include internal hemorrhagic pachymeningitis (chronic subdural hematoma), denegeration of the corpus callosum (Marchiafava-Bignami syndrome), and acute hemorrhagic polioencephalitis (Wernicke's syndrome) in which there is congestion and hemorrhage into the gray matter of the brain stem and hypothalamus, especially about the mammillary bodies. Wernicke's syndrome is characterized by ophthalmoplegia, ataxia, nystagnus and peripheral neuropathy. It and Korsakoff's psychosis in which there is disorientation, impairment of memory, confabulation and, at times, polyneuritis, result from nutritional deficiencies. Other clinical manifestations of alcoholism include delirium, dementia, pseudotabes and psychoses characterized by anxiety, feelings of inadequacy, depression, emotional instability, negativism and paranoia. Some of the neuromuscular abnormalities noted in the alcoholic may be due to the reduced magnesium content of the serum.

Liver. Both the ingestion of large quantities of ethanol and dietary deficiency produce liver damage but the specific contribution of these factors to hepatic disease in the alcoholic is still debated as is the role of the fatty liver and alcoholic hepatitis in the development of cirrhosis. Some claim that the association in man between the chronic consumption of alcohol and liver injury is a result of an induced or relative multifactorial dietary deficiency. Although chronic malnutrition may exacerbate the liver injury induced by alcohol there is good evidence to indicate that alcohol is a hepatotoxin independent of nutritional factors.

The ultrastructure of the fatty liver associated with chronic alcoholism consists of conspicuous hepatic steatosis with variable

degrees of hepatic inflammation and fibrosis. There are degenerative changes in the liver cells with the appearance of hyaline "Mallory bodies." Under the electron microscope, in addition to the accumulation of fat droplets in the cytoplasm, areas of focal cytoplasmic degeneration appear. The most striking changes occur in the mitochondria, which are enlarged and disrupted, and the endoplasmic reticulum and ribosomes are abnormal. The latter changes are observed even in cases where fatty metamorphosis is minimal. The hepatic steatosis and ultrastructural changes are produced rapidly in man by isocaloric substitution of alcohol for carbohydrate and are not prevented by excess dietary protein, a decreased fat intake, or variations of the type of fat ingested.

Transient hyperlipemia, jaundice and hemolytic anemia (Zieve's syndrome) associated with fatty liver and cirrhosis is observed in alcoholics with hepato-pancreatic damage.

Heart. Heart disease was first ascribed to chronic alcoholism by Walshe in 1872. Recent studies indicate that the metabolism of the heart may be deranged in the alcoholic with disruption of cytoplasmic and mitochondrial structures and the development of cardiomyopathy and heart failure. The occurrence of "Munich beer-drinker's" heart disease is also attributable to alcohol but the more acutely developing fatal heart disease noted in certain areas in heavy beer drinkers during recent years is believed to be due to cobalt poisoning.

Infusion of alcohol into dogs has demonstrated a release of potassium, magnesium, phosphate and transaminase into the coronary-sinus blood, deterioration of the ventricular function curve, an increase in left ventricular work load, and a decreased up-take of free fatty acids. These changes as well as the morphologic disturbances noted in the chronic alcoholic support the concept that alcohol may be an etiologic and aggravating factor in heart failure.

Muscles. In addition to nutritional polyneuropathy with atrophy of the muscles secondary to degeneration of the peripheral nerves, a primary affection of the muscles is at times associated with chronic alcoholism. This myopathic syndrome is accompanied by severe pain, tenderness and edema of the muscles, and

in most cases by renal dysfunction. There is degeneration of muscle fibers with characteristic biochemical abnormalities including the appearance of myoglobin and related proteins in the urine, an increased serum creatine phosphokinase activity, and a poor lactic acid response to ischemic exercise. The condition resembles hereditary phosphorylase deficiency (McArdle's syndrome) except that it is reversible. A chronic progressive myopathy associated with alcoholism has also been described.

Pathogenetic mechanisms assumed to be responsible for the above-described muscle abnormalities include: depression of glycolytic enzymes by ethanol or its metabolites; a direct toxic effect of alcohol on the muscle cell envelope or mitochondria; magnesium and thiamine deficiency; and interference with the metabolism of myoglobin.

Delirium Tremens. A characteristic syndrome associated with chronic alcoholism and a consequence of the direct effects of alcohol rather than of the associated nutritional deficiency is delirium tremens. This condition is characterized by tremor, perspiration, sleeplessness, fear, excitement, and hallucinations which differ from other hallucinations of insanity in consisting of the multiple appearance of the same object. These objects are often animals, such as snakes, rats, dogs, *etc.* Delirium tremens follows an absolute or relative abstinence from alcohol and is produced by a rapidly falling blood alcohol level. The syndrome resembles that which follows abstinence from barbiturates in subjects chronically addicted to these drugs. The severity of the symptoms depends upon the duration of the addiction to alcohol; the relative reduction in alcohol intake (despite continued drinking) determines whether or not the syndrome will appear. Alcohol apparently can produce both tolerance and physical dependence similar to that induced by the opiates and barbiturates. Edema or "wet brain" are unlikely causes of the symptoms, but represent probably a terminal event in fatal cases. In most patients the cerebrospinal fluid pressure is normal and cerebral edema is not observed in many patients.

An attack of delirium tremens usually continues for 3 to 5 days but patients may die in a state of hyperthermia with vascular collapse, coma and convulsive seizures. Others may die suddenly,

possibly as a consequence of fat embolism. Some die with a fatty liver. It was formerly believed that magnesium deficiency might be responsible for the syndrome since it resembles that seen in such deficiency but this view has not been confirmed by later work. Although alcohol may alleviate the symptoms it is not a recommended form of therapy since it aggravates other conditions and it is difficult to maintain a steady blood level. Paraldehyde (4 to 12 ml. by mouth or rectum), barbiturates in large doses, bromides (1 gram every 1 to 4 hours), chloral (at night), vitamins, and general symptomatic care constitute the best therapeutic regimen. The phenothiazine drugs have been recommended but their extolled virtues have been questioned. Adequate hydration and electrolyte replacement intravenously are important. The adrenal corticoids are of questionable value. The use of 8 grams of magnesium sulfate, intramuscularly, daily in divided doses for the first 3 days and 4 grams daily for 2 to 4 days thereafter has also been recommended in more seriously ill patients.

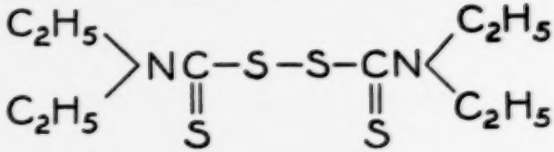
Treatment. The treatment of acute alcoholic intoxication consists of evacuating the stomach by means of the stomach tube and the administration of one of the tranquilizing drugs described in Chapter 9. In cases of respiratory depression, the injection of stimulants (caffeine) or the inhalation of 90 per cent oxygen and 10 per cent carbon dioxide may be indicated. Amphetamine may also be indicated for its stimulating effects in case of profound coma.

The treatment of chronic alcoholism is a difficult problem requiring psychotherapy for the underlying personality disorder responsible for the craving for drink. Attempts have been made to induce a conditioned reflex distaste for alcohol by simultaneously administering apomorphine, which causes nausea, with each drink. Amphetamine has also been used to overcome the depression following the withdrawal of the alcohol. Institutions and organizations which invoke the additional factors of spiritual inspiration and mass psychology are also helpful. Of these *Alcoholics Anonymous* has proved most effective. The therapeutic effectiveness of this organization has been attributed to its use of a spiritual force to attack the narcissism of the alcoholic addict. By accepting the view that he is sick and that his drinking is the

manifestation of a deep-seated compulsion, the addict is relieved of moral responsibility for his past drinking behavior and is encouraged to strive for 24 hours' sobriety.

Disulfiram (Antabuse), tetraethylthiuram disulfide, is used in the treatment of alcoholism because of the disagreeable symptoms which it induces when ingested with alcohol.

Since minute amounts of the drug inhibit liver aldehyde oxidase and elevate blood acetaldehyde levels, the disagreeable symptoms elicited have been attributed to the accumulation of this metabolic degradation product of alcohol. However, this theory is unlikely since disulfiram fails to inhibit the removal of injected acetaldehyde from the blood as rapidly as anticipated by this assumption. The mechanism of action of disulfiram depends more likely upon the inhibition of certain enzymes, since it forms a tight complex with copper as does also its reduction product, diethyldithiocarbamate. Disulfiram also oxidizes reduced glutathione rapidly and might therefore oxidize the sulfhydro-groups of enzymes. Disulfiram also interferes with most of the enzymes which oxidize or otherwise dispose of acetaldehyde, namely, aldehyde oxidase, xanthine oxidase, aldehyde dehydrogenase and glyceraldehyde-3-phosphate dehydrogenase. Its action in association with alcohol as well as its intrinsic toxicity are probably a consequence of these multiple actions.



Disulfiram

Disulfiram is administered orally in an initial dose which should not exceed 0.5 gram daily. No alcoholic beverage should have been consumed for at least 12 hours before administering the drug. The usual maintenance dose is about 0.25 gram, ranging from 0.125 to 0.5 gram daily, and should be sufficient for eliciting flushing of the face after ingesting 15 ml. of whiskey or other beverages containing 7.5 grams alcohol. Therapy is con-

tinued uninterruptedly until the patient is capable of maintaining self-control over his alcoholic tendencies.

Disulfiram is absorbed slowly from the intestinal tract and must be taken at least 12 to 24 hours prior to a test dose of alcohol to produce the desired unpleasant effects. It is also excreted slowly and symptoms have followed the ingestion of alcohol a week after a single dose of the drug.

Within 5 to 15 minutes following the ingestion of alcohol patients treated with disulfiram manifest flushing, sweating, palpitation, dyspnea, hyperpnea, tachycardia, hypotension, nausea and vomiting. Drowsiness follows with recovery after a period of sleep. Cardiovascular collapse and other serious side-effects may occur and have resulted in fatalities. The drug should be used only in association with other measures leading to the physical, emotional and social rehabilitation of the alcoholic, as the use of the drug alone provides little chance for a cure.

Citrated calcium carbimide (Temposil) resembles disulfiram in action and has also been used in the treatment of chronic alcoholism. It is less unpleasant to take than disulfiram and reactions to the drug may be controlled by the intravenous administration of an antihistaminic agent.

Therapeutic Uses

Hippocrates noted that "wine drunk with an equal quantity of water puts away anxiety and horrors" and Heberden in 1786 referred to "the relief afforded by wine and spiritous cordials" in angina pectoris. It is now apparent that any beneficent effect of alcohol in therapeutics is dependent on its sedative action in promoting a sense of well-being. In elderly individuals, for example, insomnia, restlessness and nervousness may often be allayed by the judicious use of an alcoholic beverage. Alcohol, however, has no specific therapeutic virtue and it has been replaced clinically by the more effective sedatives and hypnotics to be described later. Its use is contraindicated in cardiac, renal and hepatic disease, in gastrointestinal disturbances, and in epilepsy.

Alcohol is used externally in dilute solution (25 to 30 per cent) as a cooling application to the skin. In preventing bedsores,

in which it is often applied in order to harden the epidermis, a concentration of 50 per cent is recommended. As an antiseptic applied to the skin, it is used as a 70 per cent by weight solution. When it is kept from evaporation, it acts as a *rubefacient* and *irritant*. Its use to wash the skin and hands before operations arises from its power of cleansing the skin and removing oils and fats as well as from its disinfectant action. Alcohol is useful locally in the treatment of phenol burns, but it should be washed off immediately with water, else it does more harm than good. Its use is contraindicated in a lavage after phenol has been swallowed.

Strong alcohol (80 per cent or more) may be injected into nerves or ganglia for the relief of neuralgia, sciatica, and similar disorders and leads to degeneration of the nerve fibers and paralysis of sensation and motion which lasts until the nerve fibers are regenerated after several months. The pain disappears until this restoration is complete and sometimes permanently. The local nerve destruction arises from the precipitation of proteins and the solution of lipids.

Alcohol is used extensively as a *vehicle* for the preparation of elixirs, tinctures, and fluid extracts of medicinal agents.

Alcohol has been injected intravenously to induce general anesthesia but its use in this way is generally limited to produce analgesia prior to and following surgery. For this purpose, a 5 or 10 per cent solution of alcohol in a 5 per cent glucose or isotonic saline solution containing the 4 principal members of the vitamin B complex is administered by intravenous drip until the desired degree of analgesia is attained. For complete narcosis, 2 to 2.5 ml. of alcohol per kg. of body weight is necessary.

Alcohol (50 ml. of a 7 per cent solution) is administered orally as a test breakfast in evaluating gastric secretion. It may be inhaled to lower surface tension in pulmonary edema. For the latter purpose, a mixture of 0.01 per cent Silicone, 0.75 per cent Superinone, 1 per cent glycerol and 1 per cent potassium bicarbonate is generally preferred.